

REMARKS

Claims 17-37 are withdrawn from consideration due to the restriction requirement issued on March 7, 2006. In this paper, Applicants have amended claims to more precisely define the subject matter claimed. In addition, 5 and 8 have been cancelled.

Claim 1 has been amended to recite “[a] fusogenic vesicle encapsulating at least one therapeutic or immunologically active substance, said fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature, pH, and cell type specificity.” Support for this amendment is found in claims 5, 7, and 8 as originally filed. Support is also found, for example, in paragraphs [0026] and [0027] of the specification.

Claims 6, 9, have been amended to correct claim dependency.

Claim 6 has also been amended to recite wherein the at least two different fusion proteins cause fusion at different temperatures. Support for the amendment is found in claim 6 as originally filed and, for example, in paragraph [0026].

Claim 7 has been amended to recite “[t]he fusogenic vesicle according to claim 1, wherein at least one of the fusion proteins is cell type specific.” Support for this amendment is found in claim 1 as originally filed and, for example, in paragraph [0027] of the specification.

Claim 10 has been amended to clarify the Markush group. Claim 11 has been amended to recite “further comprising lipids derived from the group consisting of glycolipids, phospholipids, cationic lipids, synthetic lipids, and cholesterol.” Claim 12 has been amended to recite “wherein the lipids comprise POPC and DDAB. Claim 13 has been amended to recite

“further comprising lipids derived from a virus selected from the group consisting of influenza, VSV, SFV, Sendai and HIV virus.” Claim 14 has been amended to recite wherein the lipids are derived from influenza virus.” Claim 16 has been amended to recite “further comprising a cell-surface receptor, cytokine, growth-factor, antibody, or antibody fragment.” Support for the amendments to claims 10-14 and 16 is found, for example, in the respective claims as originally filed.

Rejection under 35 U.S.C. §112, Second Paragraph

Claims 1-16 and 38 stand rejected under 35 U.S.C. §112, second paragraph, for reciting “distinct fusion characteristics.” The Office Action stated that the recitation could be interpreted as requiring more than one type of fusion protein, wherein the different types have different fusion characteristics, or as requiring more than one fusion protein of a single type that has detectable (“distinct”) fusion characteristics.

Applicants have followed the Examiner’s guidance and amended claim 1 to recite “comprising at least two different viral fusion proteins (. . .) and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature, pH, and cell type specificity” in order to clarify that the vesicle has more than one type of fusion protein, wherein the different types have different fusion characteristics. Because claims 2-4, 6, 7, 9-16 and 38 depend, either directly or indirectly, from claim 1, they also incorporate the clarifying language.

Claims 3 and 4 stand rejected for reciting “the encapsulated therapeutic or immunologically active substance” without antecedent basis. Applicants have amended claim 1 to delete the wording “capable of,” such that the claim now encompasses a fusogenic vesicle encapsulating a therapeutic or immunologically active substance. With this amendment, claim 1

now provides proper antecedent basis for dependent claims 3 and 4, and thus applicants believe the rejection to be moot.

Claims 1-4, 6, 7, 9-16 and 38 satisfy the requirements of 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. §112, First Paragraph

Claims 1-16 and 38 are rejected under 35 U.S.C. §112, first paragraph as being indefinite for failing to comply with the written description requirement.

Claim 1 has been amended to recite “said fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH.” Based on the description provided in paragraphs [0021], [0026], [0027], [0032], and in the Examples, claim 1 as amended satisfies the written description requirement. Because claims 2-4, 6, 7, 9-16 and 38 depend, either directly or indirectly, from claim 1, they also incorporate the clarifying language.

Claim 7 has been amended to recite “[t]he fusogenic vesicle according to claim 1, wherein at least one of the fusion proteins is cell type specific.” Viral fusion proteins that display cell type specificity are well known to those of ordinary skill in the art. For example, paragraph [0027] of the specification teaches that the gp120 protein of HIV binds to CD4 on T lymphocytes and cells of the monocyte/macrophage lineage and can be used to target delivery of therapeutic substances to specific cell types.

Claims 1-4, 6, 7, 9-16 and 38 satisfy the requirements of 35 U.S.C. §112, first paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. §102(b)

Gunther-Ausborn, et al. as evidenced by Junankar, et al and Blough.

Claims 1, 3-9, 11, 13, 16, and 38 are rejected under 35 U.S.C. §102(b) as being anticipated by Gunther-Ausborn, *et al.* as evidenced by Junankar, *et al* and Blough.

Claim 1 has been amended to recite “[a] fusogenic vesicle encapsulating at least one therapeutic or immunologically active substance (. . .)”

Gunther-Ausborn, *et al.* describe the analysis of the kinetics of fusion of reconstituted viral membranes with erythrocyte ghosts.

There is no disclosure or suggestion in Gunther-Ausborn, *et al.* of fusogenic vesicles encapsulating at least one therapeutic substance as claimed in claim 1. Claims 3-4, 6, 7, 9, 11, 13, 16, and 38 are ultimately dependent upon claim 1. Therefore, claims 1, 3-4, 6, 7, 9, 11, 13, 16, and 38 are novel over Gunther-Ausborn, *et al.* as evidenced by Junankar, *et al* and Blough. Accordingly, Applicants respectfully request withdrawal of the rejection.

Karlsson, et al as evidenced by Hoekstra, et al

Claims 1, 3-8, 16, and 38 are rejected under 35 U.S.C. §102(b) as being anticipated by Karlsson, *et al* as evidenced by Hoekstra, *et al.*

Claim 1 is drawn to a fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH.

Karlsson, *et al* describe a second-step virus binding receptor found in nature (Abstract). According to Karlsson, *et al.*

[i]t is contemplated that it may be possible to select binding proteins or glycoproteins from the viruses in the manner described above which may be used for targeting drugs to specific cells within an organism. For instance, a liposome (lipid vesicle) may be equipped with, e.g., a monoclonal antibody with specificity for a certain target cell (for instance a tumor cell or a cell carrying intracellular parasites). To avoid being eventually inactivated through endocytotic uptake to the lysosomes, the liposome may also be tagged with the viral component recognizing the second-step receptor. In this way, the established virus mechanism for penetration may be employed as part of a vehicle for carrying a toxic drug. The liposome may be exchanged with a direct chemical coupling of antibody (first-step) and viral component (second-step) with the active subunit of a bacterial toxin exerting its actions only inside the cell (see reference 12).

(Karlsson, *et al* col. 17, lines 37-54).

There is no disclosure or suggestion by Karlsson, *et al.* for a fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH as claimed in claim 1. Claims 3, 4, 6, 7, 16, and 38 are ultimately dependent upon claim 1. Therefore, claims 1, 3, 4, 6, 7, 16, and 38 are novel over Karlsson, *et al* as evidenced by Hoekstra, *et al.* Accordingly, Applicants respectfully request withdrawal of the rejection.

Walti, et al

Claims 1-11, 13-16, and 38 are rejected under 35 U.S.C. §102(b) as being anticipated by Walti, *et al.*

Claim 1 is drawn to a fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH.

Walti, *et al* described positively charged virosomes that contain cationic and/or polycationic lipids, at least one viral fusion peptide and preferably at least one cell-specific marker. (Abstract). According to Walti, *et al* the term “fusion peptide” “refers to peptides or proteins capable of inducing and/or promoting a fusion reaction between the virosome membrane and a lipid membrane of a target cell.” (Walti, *et al* col. 8, lines 10-13). Furthermore, according to Walti, *et al*

Instead of or in addition to influenza virus hemagglutinin, the hemagglutinins from other viruses may also be suitably used as fusion peptides (proteins) for the instant virosomes as long as they exert substantially the same pH-mediated cell penetration mechanism as the influenza hemagglutinin. Candidate hemagglutinins include, for example, rhabdovirus, parainfluenza virus type III, Semliki Forest virus and togavirus, as disclosed in U.S. Ser. No. 07/930,593, now U.S. Pat. No. 6,040,167 (assignee: NIKA HEALTH PRODUCTS LTD.), incorporated herein by reference. (Emphasis added).

(Walti, *et al* col. 8, lines 31-35).

There is no disclosure or suggestion by Walti, *et al* of fusogenic vesicles comprising at least two different viral fusion proteins wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH. Claims 2-4, 6, 7, 9-11, 13-16, and 38 are ultimately dependent upon claim 1. Therefore, claims 1-4, 6, 7, 9-11, 13-16, and 38 are novel over Walti, *et al*. Accordingly, Applicants respectfully request withdrawal of the rejection

Rejection under 35 U.S.C. §103(a)

Claims 1, 11, and 12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Walti, *et al* in view of Wheeler, *et al*.

Claim 1 is drawn to a fusogenic vesicle comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV,

SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH.

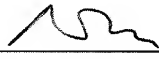
The combined teachings of Walti, *et al* in view of Wheeler, *et al* do not render claims 1, 11, or 12 obvious because the combined teachings fail to provide a suggestion or motivation to prepare the claimed fusogenic vesicles. There is no suggestion of motivation in the combined teachings of Walti, *et al* and Wheeler, *et al* to prepare fusogenic vesicles comprising at least two different viral fusion proteins wherein the fusion proteins are derived from the group consisting of influenza, VSV, SFV, Sendai and HIV viruses and wherein the at least two different types of fusion proteins have different fusion characteristics selected from the group consisting of temperature and pH. Claims 11 and 12 are dependent upon claim 1. Therefore, claims 1, 11, and 12 are non-obvious over Walti, *et al* in view of Wheeler, *et al*. Accordingly, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested. If the Examiner has any questions, the Examiner is invited to call Applicants' representative directly at (212) 969-3000.

Respectfully submitted,

Proskauer Rose LLP

By: 
Rebekka C. Noll
Reg. No. 46,962

Date: January 22, 2006
Proskauer Rose LLP
1585 Broadway
New York, NY 10036-8299
Tel: (212) 969-3000
Fax: (212) 969-2900